

## REMARKS

Applicants respectfully request reconsideration of the present application in view of reasons that follow.

### **I. Status of the claims**

Claims 23-32 were previously canceled without disclaimer or prejudice thereof.

No changes to the claims are made in this reply. Accordingly, claims 1-22 and 33-42 are pending in the application.

### **II. Claim rejection – 35 U.S.C. § 103(a)**

Claims 1-22 and 33-42 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over the combination of two primary references: U.S. Publication No. 2003/0179916 (Magnuson) and U.S. Patent No. 6,146,881 (Hering). Additional secondary references (U.S. Publication No. 2001/0019845 [Beinert], U.S. Patent No. 4,210,724 [Sogi], and U.S. Patent No. 6,064,754 [Parekh]) are cited in conjunction with Magnuson and Hering to allegedly render obvious various dependent claims. *See* Office Action at pages 3-12. Applicants respectfully traverse this ground for rejection.

#### **A. Magnuson in view of Hering**

Claims 1, 2, 5, 6, 10, 18-22 and 36-42 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Magnuson in view of Hering. Applicants respectfully traverse this ground for rejection.

#### **1. Magnuson teaches away from the claimed invention**

Claim 1 is directed to a method for picking cell colonies. This is done by aspiration into a hollow pin. The hollow pin has an inside diameter that is greater than the size of the cell colonies. The significance of this is that an *entire colony* can be aspirated into the pin without damage.

Claim 10 is directed to an apparatus for picking animal cell colonies. The apparatus includes at least one hollow pin, wherein the at least one hollow pin comprises an inner pin and an outer pin, and the inner pin is recessed axially inside an end of the outer pin. The apparatus enables aspirating an animal cell colony into the inner pin.

Magnuson is also directed to a method for picking cell colonies based on hollow-pin aspiration. However, unlike the claimed invention, Magnuson's scheme requires the hollow pin to have a diameter which is *smaller* than the size of the cell colonies. This requirement by Magnuson is necessary to enable the pin to form an air-tight seal with the colony for the aspiration, for example as described in Magnuson at paragraph [0127] and [0170]:

For example, if the removal is to be exclusively via aspiration techniques, a tip can be designed such that it can form an essentially airtight seal with the colony or cell, making the removal of the cell or colony more efficient.

Since the pipette diameter is smaller than the colony diameter, the pipette must be moved incrementally to aspirate the entire colony.

(Magnuson at paragraphs [0127] and [0170]). Thus, only *a portion* of the colony is aspirated.

Additionally, Magnuson specifically explains at paragraph [0172] that the pin into which the colony portion is aspirated *must* be smaller than the colony for the Magnuson device to work.

When the 0.2 mm capillary pipette was placed directly on top of the colony, it took 25-40 mmHg of vacuum with an inline 0.2  $\mu$ M filter to lift up the portion of the colony contacting the capillary tip. Without the inline filter, the vacuum needed was only 15-25 mmHg. If some side-to-side scraping motion was applied to pre-lift the colony, less than 5 mmHg was needed to aspirate the cells. *When this experiment was repeated with a 0.4 mm diameter pipette, a good seal could not be maintained between the edge of the pipette and the colony. Consequently, a large amount of medium was aspirated instead of the colony.* The results of this experiment indicate that cells can be picked with low vacuum and standard capillary pipettes.

(Magnuson at paragraph [0172], emphasis added).

Thus, Magnuson teaches *away* from the claimed invention in teaching that one of Applicants' required claim elements – i.e., a hollow pin having a diameter *larger* than the size of the cell colonies - is undesirable and if present would make the device of Magnuson unworkable. Hering does not remedy this deficiency of Magnuson.

**2. There is no motivation to modify the aspiration pin of Magnuson with the perfusion ring of Hering**

Specifically, Hering describes a scheme for handling cells in a liquid bath. A “perfusion ring” is first placed in the bath in sealed contact with the floor of the bath to isolate a portion of the liquid (*see* col. 4, lines 48-51 and also col. 9 lines 5-6). A conventional syringe/pipette is used to withdraw cells or fluid from the contents inside the perfusion ring, or to add fluid to the contents inside the perfusion ring. The function of the perfusion ring is to prevent cross-contamination between the liquid inside the perfusion ring and the rest of the bath during cell handling.

The Office Action concedes that the picking apparatus of Magnuson includes neither a hollow pin having a diameter greater than the colony to be picked nor a hollow pin comprising an inner and an outer pin. However, the Office Action asserts that the disclosure of Hering cures the deficiency of Magnuson. (*See* Office Action at pages 4-5). Applicants respectfully disagree.

As described above, Magnuson does not disclose an aspirating pin having a diameter greater than the colony to be picked. Furthermore, the skilled artisan would not consider increasing the diameter of the aspirating pin in Magnuson to a size greater than the colony to be picked. This is because Magnuson clearly explains that the aspirating pin must be smaller than the colony for the Magnuson device to work (*e.g.*, *see* Magnuson at paragraph [0172]). This was also discussed in the last reply, dated December 1, 2008. The Examiner indicated in this reply that such reasoning was persuasive. (*See* Office Action at page 12 at Response to Argument).

Thus, the Office Action asserts that although it *would not* be obvious to increase the diameter of the aspirating pin in Magnuson, it *would* be obvious to modify Magnuson to add

the perfusion ring of Hering. (Office Action at page 5). The perfusion ring would then allegedly render the present claims obvious because the perfusion ring (added to the aspirating pin) of the Magnuson/Hering combination would be larger than a colony. (Office Action at pages 5). The Office Action also asserts that “Hering teaches that the use of an additional outer hollow pin of a large diameter is beneficial because it can be used to isolate a particular cell collection area during aspiration,” and that the “outer hollow pin would serve to define a discrete treatment area within a liquid bath, thus preventing contamination during collection.” (Office Action at page 5). Applicants respectfully disagree.

The skilled artisan would not consider adding a perfusion ring to Magnuson. This is because the perfusion ring of Hering is for isolating fluid containing the object to be picked from the remainder of the liquid bath to avoid cross-contamination. However, there would be no need for this kind of isolating seal in Magnuson. This is because the aspirating pin of Magnuson already provides an isolating seal. As is clearly explained in Magnuson at paragraph [0172], the aspirating pin forms a tight seal over the portion of the colony to be aspirated. Thus the aspirating pin already isolates the medium containing the portion of the colony to be aspirated from the remainder of the medium. Any additional perfusion ring in Magnuson would therefore be wholly redundant and would serve no purpose. Accordingly, there is no reason, and so no motivation, for the skilled and creative artisan to add a perfusion ring to Magnuson.

**3. Modification of Magnuson with the perfusion ring of Hering would not yield the method recited in claim 1**

Moreover, even if a perfusion ring was added to the device of Magnuson, the claimed invention would not be obtained. This is because it is simply not possible for any perfusion ring added to Magnuson to read on the hollow pin of claim 1.

A perfusion ring is for isolating a colony to be picked from the remainder of the sample medium. The perfusion ring plays no role in the colony aspiration itself. Claim 1 however recites “aspirating the animal cell colony into the hollow pin.” Any perfusion ring added to Magnuson cannot therefore read onto the hollow pin of claim 1, because in such a fictitious combination the aspiration would not be into the perfusion ring. The aspiration

would still be into Magnuson's hollow pin having a diameter less than the colony size. The addition of a perfusion ring does not change this.

Accordingly the skilled artisan would not be motivated to add the perfusion ring of Hering to Magnuson, and furthermore such a combination does not read on the claimed invention.

#### **4. Summary**

For at least the reasons stated above, independent claims 1 and 10 are non-obvious over Magnuson in combination with Hering. As such, claims 1, 2, 5, 6, 10, 18-22 and 36-42 are patentable and reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a) is respectfully requested.

#### **B. Rejection over Magnuson, Hering and Beinert**

Claims 3, 13 and 33 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Magnuson and Hering as applied to claims 1 and 10, and further in view of Beinert. Office Action at page 6. Applicants respectfully traverse this ground for rejection.

The failure of Magnuson and Hering to teach or suggested the invention of claims 1, 2, 5, 6, 10, 18-22 and 36-42 is demonstrated above. The additional reference, Beinert, does not remedy the deficiencies of Magnuson and Hering. Beinert discloses a freely traversable metering head with numerous metering devices. Beinert fails to disclose or suggest a method or apparatus for picking animal cell colonies as claimed in the application.

Therefore, claims 3, 13 and 33 are patentable under 35 U.S.C. § 103(a) over the combination of Magnuson, Hering and Beinert, and reconsideration and withdrawal of the rejection is respectfully requested.

#### **C. Rejection over Magnuson, Hering and Sogi**

Claims 4, 11, 12, 34 and 35 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Magnuson and Hering as applied to claims 1 and 10, and further in view of Sogi. (Office Action at page 7). Applicants respectfully traverse this ground for rejection.

The failure of Magnuson and Hering to teach or suggest the invention of claims 1, 2, 5, 6, 10, 18-22 and 36-42 is demonstrated above. The additional reference, Sogi, does not remedy the deficiencies of Magnuson and Hering. Sogi is directed to an apparatus for liquid disposal and distribution for use in automatic culture and fails to disclose or suggest a method or apparatus for picking animal cell colonies as claimed in the application. Therefore, claims 4, 11, 12, 34 and 35 are patentable under 35 U.S.C. § 103(a) over the combination of Magnuson, Hering and Sogi, and reconsideration and withdrawal of the rejection is respectfully requested.

**D. Rejection over Magnuson, Hering and Parekh**

Claims 4, 7-9, 11, 12 and 14-17 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Magnuson and Hering as applied to claims 1 and 10, and further in view of Parekh. Office Action at page 9. Applicants respectfully traverse this ground for rejection.

The failure of Magnuson and Hering to teach or suggest the invention of claims 1, 2, 5, 6, 10, 18-22 and 36-42 is demonstrated above. The additional reference, Parekh, does not remedy the deficiencies of Magnuson and Hering. Parekh is drawn to computer-assisted methods and apparatus for identifying, selecting and characterizing biomolecules in a biological sample. However, Parekh fails to disclose or suggest a method or apparatus for picking animal cell colonies as claimed in the application. Therefore, claims 4, 7-9, 11, 12 and 14-17 are patentable under 35 U.S.C. § 103(a) over the combination of Magnuson, Hering and Parekh, and reconsideration and withdrawal of the rejection is respectfully requested.

**III. Conclusion**

The present application is now in condition for allowance. Favorable reconsideration of the application is respectfully requested.

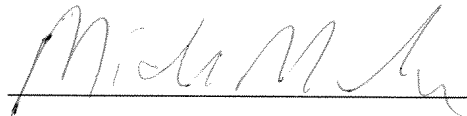
The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by the credit card payment instructions in EFS-Web being incorrect or absent, resulting in a rejected or incorrect credit card transaction, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorize payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date July 16, 2009

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